Translation

PCT/JP2003/004614

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference PCT196 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/JP2003/004614 | International filing date (*day/month/year*) 11 April 2003 (11.04.2003) | Priority date (*day/month/year*) 11 April 2002 (11.04.2002) |
| International Patent Classification (IPC) or national classification and IPC C07K 7/08, 1/06, 14/00 // C12N 15/09 | | |
| Applicant MOCHIDA PHARMACEUTICAL CO., LTD. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 16 October 2003 (16.10.2003) | 06 May 2004 (06.05.2004) |
| Name and mailing address of the IPEA/JP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/004614

## I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-28 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-28 | NO |
| Industrial applicability (IA) | Claims | 1-28 | YES |
| | Claims | | NO |

2. Citations and explanations

Documents:

1. Niidome T, et al., Binding of cationic alpha-helical peptides to plasmid DNA and their gene transfer abilities into cells.
   J Biol Chem. 1997 Jun 13, Vol. 272, No. 24, p. 15307-15312
2. WO 01/49324 A2 (NOVARTIS AG) July 12, 2001
3. Sakaibara T, et al., Doxorubicin encapsulated in sterically stabilized liposomes is superior to free drug or drug-containing conventional liposomes at suppressing growth and metastases of human lung tumor xenografts.
   Cancer Res. 1996 Aug 15, Vol. 56, No. 16, p. 3743-3746
4. Kazuo MARUYAMA, "PEG-liposomes ni yoru DDS no Rinsho Oyo," Japanese Journal of Clinical Medicine. 1998, Vol. 56, No. 3, p. 632-637
5. Maruyama K, et al., Targetability of novel immunoliposomes modified with amphipathic poly(ethylene glycol)s conjugated at their distal terminals to monoclonal antibodies.
   Biochim Biophys Acta. 1995 Mar 8, Vol. 1234, No. 1, p. 74-80
6. WO 00/44348 A2 (UNIV ILLINOIS FOUND) August 3, 2000

(Continued)

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V. 2:

•Claims 1-28

Document 2 states that stabilization is greatly enhanced when a vector used for gene therapy is modified by polyethylene glycol (PEG). In addition, as described in documents 3-6, the stabilization of a substance and delivery of that substance to a desired site by encapsulating it in a PEG-modified liposome in order to enhance its action was widely known by persons skilled in the art before the priority date of this application.

Thus, persons skilled in the art can easily conceive of modifying with PEG the peptide having an α-helix structure described in document 1 for delivering a gene into a cell to enhance its stability and physiological activity. Furthermore, in so doing, persons skilled in the art can substitute or add amino acids in consideration of the hydrophilicity or hydrophobicity of the peptide.

Moreover, this examination finds no particularly outstanding effect is provided by adopting the constitution of the inventions in the above claims.

As a result, this examination finds that persons skilled in the art could easily prepare the inventions of the above claims based on the descriptions in documents 1-6.